

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 03/03444

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G06F17/50 G06F19/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPQ-Internal, BIOSIS, WPI Data, MEDLINE, EMBASE, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| A | US 6 081 766 A (LATHROP RICHARD H ET AL) 27 June 2000 (2000-06-27) | |
| A | BOER D R ET AL: "Superstar: comparison of CSD and PDB-based interaction fields as a basis for the prediction of protein-ligand interactions" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 312, no. 1, 7 September 2001 (2001-09-07), pages 275-287, XP004466135 ISSN: 0022-2836 | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

13 May 2004

Date of mailing of the international search report

08/06/2004

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | <p>LUQUE IRENE ET AL: "Structure-based thermodynamic design of peptide ligands: Application to peptide inhibitors of the aspartic protease endothiapepsin" PROTEINS STRUCTURE FUNCTION AND GENETICS, vol. 30, no. 1, 1 January 1998 (1998-01-01), pages 74-85, XP002280198 ISSN: 0887-3585</p> <p>-----</p> | |

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 30
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(v) PCT - Presentation of information ; Rule 39.1(i) PCT - Scientific theory.
2. ☒ Claims Nos.: 30
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 30

Present claim 29 relate to a compound defined by reference to a desirable characteristic or property, namely a species and/or macromolecule identified/designed/modified/optimized by the method according any of claims 1-28. Taking the example of Aspartate proteases, claim 29 is directed to inhibitors of said protease type. The present claim does not disclose any technical feature which would characterise the species the claim is directed to. Consequently, any already known aspartate protease inhibitor would fall into the scope of present claim 29 since it is not of relevance how a known substance was identified etc.

The method of claims 1 to 28 is to be characterised as a method for molecular design which defines a chemical entity able to interact with a macromolecule compared with a mechanical entity, i.e. with a machine performing a certain mechanical action, e.g. cutting.

The "mechanical analogue" can be selected arbitrarily so that the definition of a mechanical analogue to a part of a physiologically active macromolecule (protein, nucleic acid or polysaccharide) appears to have no well defined meaning, i.e. the set of entities to be investigated is dependent upon the arbitrary view of the skilled person dealing with molecular design of a desired entity. A hydrolase might well be seen as an equivalent of a cutting machine but an oxidoreductase transferring only electrons or a proton is open to interpretation.

The applicant provided a theoretical approach how e.g. enzymes can be subdivided into functional "mechanical equivalents" which are target of calculations how these functionalities can be influenced by effectors (inhibitors etc.). The result of this theoretical approach is exemplified by the categorisation of parts of existing "sub-units" of aspartate proteases. The next step, i.e. to design effectors to these functionalities, has not been disclosed. It is not clear whether the claimed method solves the problem posed. The applicant does not provide any example which proves that the claimed method leads to a molecule with the desired properties, i.e. an inhibitor of an aspartate protease.

Taking this lack of clarity and this lack of disclosure into consideration (Articles 5 and 6 PCT), the subject-matter of the present application could only be searched with respect to the general approach and its application to the sole disclosed entities, i.e. aspartate proteases.

The retrieved prior art represents a general technical background of the art of molecular design since the concept of "mechanical equivalents" as presently disclosed appears not to be disclosed.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 03/03444

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|---------------------|
| US 6081766 A | 27-06-2000 | AU 7311994 A | 20-12-1994 |
| | | WO 9428504 A1 | 08-12-1994 |
| | | US 5703792 A | 30-12-1997 |
| | | US 5526281 A | 11-06-1996 |
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